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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/165,522	10/02/1998	ROGER J. DAVIS	10363/005001	7986

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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 06/18/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/165,522	DAVIS ET AL.	
	Examiner	Art Unit	
	Manjunath N Rao	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,18,19,23-36 and 46-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23-36 and 48* is/are allowed.

6)☒ Claim(s) *1,2,18,19,46,47 and 49-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) ✓
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request filed on 4-5-02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/165,522 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 1-2, 18-19, 23-36, 46-59 are still at issue and are present for examination.

Applicants' arguments filed on 4-5-02, paper No. 22, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

The drawings filed in the above application have been accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 46 and claim 47 depending from claim 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 46 recites the phrase "phosphorylation in the presence compared to the absence". It is unclear to the Examiner as

what comparisons are being made by the applicant in this claim. It appears that applicants are comparing the extent of phosphorylation of the JNK3 substrate in the presence and absence of the compound. If this is so, amending the claim to recite "phosphorylation in the presence of the compound compared to the phosphorylation in the absence of the compound; and..." would overcome this rejection.

Claims 50-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 50 and 51 recite the phrase "allow the interaction of". It is not clear to the Examiner as to what applicants mean by "interaction" in this claim even though ultimately, it appears that applicants compare the JNK3 activity. Literally and in the above context, with reference to JNK3, "interaction" may mean either binding, phosphorylating, activating, inactivating etc. However, among all the above plausible meanings it is not clear to the Examiner as to what exactly applicants mean by "interaction".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 18, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over McKay et al. (US 5,877,309, 3-2-1999, filed 8-13-1997). Claims 1-2 of the instant application are drawn to a

method of identifying a compound that modulates JNK3 expression. McKay et al. teach a method for assaying modulation of expression of JNK protein including JNK1, JNK2 and JNK3 (see particularly, examples 2-5). McKay et al. Also teach oligonucleotides capable of hybridizing to nucleic acids encoding JNK1-3 and modulating the expression of JNK proteins. Furthermore, McKay et al. teach that such oligonucleotides can be used to for inhibiting hyperproliferation of cells and formation , development and maintenance of tumors. However, McKay et al. do not teach specifically a peptide, peptidomimetic, a small organic molecule or a small inorganic molecule.

However, using the reference of McKay et al. it would have been obvious to one of ordinary skill in the art, especially those interested in identifying agents other than oligonucleotides, to identify small organic compounds, peptides or peptidomimetics or inorganic compounds that modulate the expression of JNK3. One of ordinary skill in the art would have been motivated to do so in view of common knowledge in the art that the oligonucleotides used as antisense is not always successful or even economical or simply to have an extensive list of compounds that could be easy to manufacture, pack, and deliver and or administer to a patient. Furthermore, McKay et al. teach that one would be motivated to do this as inhibition of JNK activity (which can be brought about by preventing its expression) results in decreased AP-1 activity leading to inhibition of abnormal cell proliferation and tumor proliferation, development and maintenance (see column 1, lines 25-30). One would have a reasonable expectation of success since McKay et al. demonstrate that it is possible to achieve above results by using antisense oligonucleotides.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

Claims 49- 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al. (EMBO Journal, Vol. 15(11):2760-2770, 1996) and McKay et al. (US 5,877,309, 3-2-1999, filed 8-13-1997) . Claims 49-59 of the instant application are drawn to a method of identifying candidate compounds for treatment of disorder related to excitotoxicity or a neuronal disorder by simply incubating JNK3 protein with JNK3 substrate (such as c-Jun) and comparing the activity (interaction) of JNK3 in the presence and absence of the compound wherein a difference in the level of JNK3 activity indicates that the compound is a candidate compound.

Gupta et al. teach the identification of JNK isoforms, including JNK3. The reference teaches that c-Jun is an established substrate for JNK3 and has a kinase activity. The reference of Gupta et al. provides assay methods for determining the activity and binding of JNK3 to its substrate. The reference does not teach the use of the same methods towards identification of compounds that modulate the activity. McKay et al. teach a method for assaying modulation of expression (which ultimately leads to reduced activity of JNK3) of JNK protein including JNK1, JNK2 and JNK3 (see particularly, examples 2-5) using oligonucleotides. Furthermore, McKay et al. teach that such oligonucleotides can be used for inhibiting hyperproliferation of cells and formation, development and maintenance of tumors. McKay et al. also teach that one of substrate of JNK3 protein is c-Jun. However, McKay et al. do not teach specifically the use of their methods for identification of a peptide, peptidomimetic, a small organic molecule or a small inorganic molecule.

Using the reference of Gupta et al. (or even that of McKay et al.) which teaches assay methods for JNK3 activity and combining it with McKay et al. which teaches that inhibiting the expression of JNK3 (which ultimately leads to reduced activity of JNK3) leads to inhibition of hyperproliferation of cells and formation, development and maintenance of tumors, it would have been obvious to one of ordinary skill in the art, especially those interested in identifying agents other than oligonucleotides, to use the assay methods provided by either of the above two references to identify compounds that interact with JNK3 (either by inhibiting expression or activity such as phosphorylation of JNK substrate or by binding to JNK3). One of ordinary skill in the art would have been motivated to do so in view of common knowledge in the art that the oligonucleotides used as antisense is not always successful or even economical or simply to have an extensive list of additional compounds that could be easy to manufacture, pack, and deliver and or administer to a patient maintaining a tumor. Furthermore, McKay et al. teach that one of ordinary skill in the art would be motivated to do this as inhibition of JNK activity (which can be brought about by preventing its expression/activity) results in inhibition of abnormal cell proliferation and tumor proliferation, development and maintenance (see column 1, lines 25-30). One would have a reasonable expectation of success since McKay et al. demonstrate that it is possible to achieve above results by using antisense oligonucleotides.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

Examiner has rejected the above claims under 35 U.S.C. 103(a) over McKay et al. and Gupta et al. because, while the preamble claims 49-52 recite method of identification of candidate compounds for treatment of an excitotoxic disorder (or neuronal disorder), the steps of

the claimed method are all directed to identification of compounds which either alter the activity or expression of JNK3, and the intended use of such compounds, once identified, does not carry any patentable weight, as the steps of the method are identical regardless of what one intends to use the selected compounds for, in the future. Furthermore, applicants may argue that the above rejection is improper as the reference of Mckay et al. or Gupta et al. does not teach the involvement of JNK3 in neuronal disorders or that compounds which modulate activity/expression of JNK3 can be used to treat neuronal disorders. Such an argument will not be persuasive to overcome the above rejection because applicants have not established any specific step of the claimed method that requires knowledge of such a relationship between JNK3 and neuronal disorders or JNK3 and excitotoxic disorders in the claims. Applicants appear to claim that any compound that simply modulates the activity/expression or interacts with JNK3 protein and its substrates is a candidate compound for treating neuronal disorders or excitotoxicity.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

Claims 23-36, 48 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.
6/17/02